(FILE 'HOME' ENTERED AT 10:23:53 ON 29 APR 2002)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 10:24:21 ON 29 APR 2002

L1 892 S BRCA1 AND (PCR OR POLYMERASE (W) CHAIN)

L2 30 S L1 AND (EXON (2A) (13 OR 22))

L3 14 DUP REM L2 (16 DUPLICATES REMOVED)

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L4 ANSWER 1 OF 5 MEDLINE DUPLICATE 1
AN 97029994 MEDLINE
DN 97029994 PubMed ID: 8875917
TI Clinical and pathological features of ovarian cancer in women with germ-line mutations of **BRCA1**.
CM Comment in: N Engl J Med. 1996 Nov 7;336(19):1455-6
Comment in: N Engl J Med. 1997 Apr 24;336(17):1254-5; discussion 1256-7
Comment in: N Engl J Med. 1997 Apr 24;336(17):1254; discussion 1256-7
Comment in: N Engl J Med. 1997 Apr 24;336(17):1255-6; discussion 1256-7
Comment in: N Engl J Med. 1997 Apr 24;336(17):1255; discussion 1256-7
Comment in: N Engl J Med. 1997 Apr 24;336(17):1256; discussion 1256-7
AU Rubin S C; Benjamin I; Behbakht K; Takahashi H; Morgan M A; LiVolsi V A; Berchuck A; Muto M G; Garber J E; Weber B L; Lynch H T; Boyd J
CS Department of Obstetrics and Gynecology, University of Pennsylvania Medical Center, Philadelphia, PA 19104, USA.
SO NEW ENGLAND JOURNAL OF MEDICINE, **(1996 Nov 7)** 335 (19) 1413-6.
Journal code: NOW; 0255562. ISSN: 0028-4793.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961114
AB BACKGROUND: We tested the hypothesis that ovarian cancers associated with germ-line mutations of **BRCA1** have distinct clinical and pathological features as compared with sporadic ovarian cancers. METHODS: We reviewed clinical and pathological data on patients with primary epithelial ovarian cancer found to have germ-line mutations of **BRCA1**. Survival among patients with advanced-stage cancer and such mutations was compared with that in control patients matched stage, grade, and histologic subtype of the tumors. A combination of single-strand conformation and sequencing analyses was used to examine the **22** coding **exons** and intronic splice-donor and splice-acceptor regions of **BRCA1** for mutations in pathological specimens. Alternatively, some patients were known to be obligate carriers of the mutant **BRCA1** gene because of their parental relationships with documented mutant-gene carriers. RESULTS: We identified 53 patients with germ-line mutations of **BRCA1**. The average age at diagnosis was 48 years (range, 28 to 78). Histologic examination in 43 of the 53 patients showed serous adenocarcinoma. Thirty-seven tumors were of grade 3, 11 were of grade 2, 2 were of grade 1, and 3 were of low malignant potential. In 38 patients, the tumors were of stage III; 9 patients (including those with tumors of low malignant potential) had stage I disease, 5 had stage IV, and 1 had stage II. As of June 1996, with a median follow-up among survivors of 71 months from diagnosis, 20 patients had died of ovarian cancer, 27 had no evidence of the disease, 4 were alive with the disease, and 2 had died of other diseases. Actuarial median survival for the 43 patients with and advanced-stage disease was 77 months, as compared with 29 months for the matched controls ($P<0.001$). CONCLUSIONS: As compared with sporadic ovarian cancers, cancers associated with **BRCA1** mutation appear to have a significantly more favorable clinical course.

L4 ANSWER 2 OF 5 MEDLINE DUPLICATE 2
AN 96225458 MEDLINE
DN 96225458 PubMed ID: 8640237
TI Mutation analysis in the BRCA2 gene in primary breast cancers.
AU Miki Y; Katagiri T; Kasumi F; Yoshimoto T; Nakamura Y
CS Department of Human Genome Analysis, Cancer Chemotherapy Center, Tokyo,

Japan.
SO NATURE GENETICS, **(1996 Jun)** 13 (2) 245-7.
Journal code: BRO; 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-D83989
EM 199607
ED Entered STN: 19960726
Last Updated on STN: 19990129
Entered Medline: 19960716
AB Breast cancer, one of the most common and deleterious of all diseases affecting women, occurs in hereditary and sporadic forms. Hereditary breast cancers are genetically heterogeneous; susceptibility is variously attributable to germline mutations in the **BRCA1** (ref. 1), BRCA2 (ref. 2), TP53 (ref. 3) or ataxia telangiectasia (ATM) genes, each of which is considered to be a tumour suppressor. Recently a number of germline mutations in the BRCA2 gene have been identified in families prone to breast cancer. We screened 100 primary breast cancers from Japanese patients for BRCA2 mutations, using PCR-SSCP. We found two germline mutations and one somatic mutation in our patient group. One of the germline mutations was an insertion of an Alu element into **exon 22**, which resulted in alternative splicing that skipped **exon 22**. The presence of a 64-bp polyadenylate tract and evidence for an 8-bp target-site duplication of the inserted DNA implied that the retrotransposal insertion of a transcriptionally active Alu element caused this event. Our results indicate that somatic BRCA2 mutations, like somatic mutations in the **BRCA1** gene, are very rare in primary breast cancers.

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 1997:146761 CAPLUS
DN 126:181894
TI A protein truncation test for **BRCA1**
AU Garvin, Alex M.; Mueller, Hj.; Scott, Rodney J.
CS Dep. Genetics, Children's Hosp., Basel, Switz.
SO Hered. Cancer, Int. Res. Conf. Fam. Cancer, 2nd (**1996**), Meeting Date 1995, 6-10. Editor(s): Mueller, Hansjakob; Scott, Rodney J.; Weber, Walter. Publisher: Karger, Basel, Switz.
CODEN: 64BIAV
DT Conference
LA English
AB The recently isolated **BRCA1** gene [1] spans 100 kb of chromosome 17q21 and contains 1,863 codons dispersed on **22 exons**. Screening for mutations in **BRCA1** by single-strand conformation polymorphism (SSCP) or sequencing requires as many as 50 PCR reactions followed by anal. of the 50 amplified products [2]. Such a work-intensive endeavor makes large-scale screening of **BRCA1** problematic. One way of reducing the amt. of work required to screen coding sequence is to perform a protein truncation test (PTT) [3], in which the coding sequence is PCR amplified with an RNA polymerase binding site attached to its 5' end. The PCR product is then used as template in a coupled in vitro transcription/translation reaction and the radiolabeled protein product is analyzed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). PTT has been successful in screening for mutations in the APC tumor suppressor gene [4]. Since 86% of all mutations found in **BRCA1** result in a truncated protein product [5], **BRCA1** is an esp. attractive candidate for screening by PTT. Below the authors will describe a PTT capable of screening the entire coding region of **BRCA1** using 7 PCR per screen. The authors also show an example of a mutation in **BRCA1** detected using this assay.

```
-12345X@PJL
@PJL JOB NAME = "MSJOB 23"
@PJL USTATUS JOB = ON
@PJL USTATUS PAGE = OFF
@PJL USTATUS DEVICE = ON
@PJL USTATUS TIMED = 30
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detected in any of the tumors, constitutional mutations were identified in four cases: two frameshifts, one nonsense mutation and one intronic base substitution 32 bp downstream of **exon 22**; RT-**PCR** experiments revealed that the single-base substitution in the intron seemed to increase the transcript lacking **exon 22**. All four cases were judged to involve truncation of the gene product. The evidence reported here supports a rather limited role of **BRCA1** in ovarian carcinogenesis in the Japanese population.

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